

## **REMARKS**

By this amendment, Applicant has canceled claims 16-20 and 23-25. New claims 26-33 have been added. Claims 26 and 30 are the new independent claims. Support for these claims is found in the specification as is discussed below. New dependent claims 27-29 are identical to canceled claims 23-25, except that they are dependent on claim 26 rather than canceled claims 16, 23 and 24. Analogously, new dependent claims 31-33 are identical to canceled claims 18-20, except that they are dependent on claim 30 rather than canceled claims 16-19. Entry and consideration of the amendment presented herein is respectfully requested. Accordingly, claims 26-33 are before the Examiner. Favorable consideration of these claims is respectfully requested.

Applicant would like to thank Examiners Oh and Kishor for granting him a telephone interview on December 16, 2005, 10:30 a.m. The discussion concentrated on rejections of claims under 35 USC 103(a) as being unpatentable over Li et al. in view of Jimenez et al. Examiner Kishor recommended, and Examiner Oh concurred, that the rejections could be overcome by replacing “comprising” with “consisting” in the independent claims and by including a range of useful heat doses.

Applicant presents with this amendment new independent claims 26 and 30 that incorporate the above recommendations by the Examiners. Claim 26 reads as follows:

“A method for protecting a human patient or a mammalian animal to be subjected to chemotherapy treatment of a tumor not residing in the scalp or other region susceptible to chemotherapy-induced alopecia of the patient or the skin of the animal against chemotherapy-induced alopecia, the protective method consisting of administering an effective heat dose to the scalp or other region susceptible to chemotherapy-induced alopecia of the patient or the skin of the animal sufficiently prior to the administration of a chemotherapeutic drug whereby hair follicles in the scalp or other region susceptible to chemotherapy-induced alopecia of the patient or the skin of the animal are heated to and maintained at a temperature of about 39-45°C during about 15-120 minutes.”

To facilitate comparison, changes made in the new claim relative to the canceled independent claim 16 are underlined, and canceled independent claim 16 is reproduced below:

“A method for protecting a human patient or a mammalian animal to be subjected to chemotherapy treatment of a tumor not residing in the scalp of the patient or the skin of the animal against chemotherapy-induced alopecia, comprising administering an effective heat dose to the scalp of the patient or the skin of the animal sufficiently prior to the administration of a chemotherapeutic drug.”

Applicant would like to provide the following explanations for the changes made: support for the substitution of “scalp” with “scalp or other region susceptible to chemotherapy-induced alopecia” is found in the specification on page 14, Lines 27-29: “A physical inducer may also be targeted to any other region of the human body susceptible to chemotherapy-induced alopecia, such as for example eyebrow, beard and mustache regions.” The term “comprising” was substituted with “the protective method consisting of” in accordance with the Examiners recommendations. Finally, an effective heat dose range was included in a “whereby” clause. Support for this addition is found in the specification on page 20, Lines 15-17: “The typical range of elevated temperatures extends from about 39°C to 45°C, and the typical duration of elevated temperature exposures is between about 2 hours and 15 min.”

The specification provides an alternative definition of effective heat dose. New independent claim 30 reproduced below is identical to claim 26, except that its “wherein” clause contains the alternative definition:

“A method for protecting a human patient or a mammalian animal to be subjected to chemotherapy treatment of a tumor not residing in the scalp or other region susceptible to chemotherapy-induced alopecia of the patient or the skin of the animal against chemotherapy-induced alopecia, the protective method consisting of administering an effective heat dose to the scalp or other region susceptible to chemotherapy-induced

alopecia of the patient or the skin of the animal sufficiently prior to the administration of a chemotherapeutic drug, wherein the effective heat dose is a dose equal or greater to that required to cause a detectable increase in the concentration of a stress protein selected from the group consisting of Hsp90, Hsp70, Hsp25-27 and P-glycoprotein in cells of hair follicles.”

Support for the wherein clause is found in the specification, beginning on page 19, Line 31: “In order to protect hair follicle cells against killing by the chemotherapeutic agent, the dose of physical inducer administered must be sufficiently high to activate the stress protein response in the follicle cells, which results in an objectively measurable increase in the concentration of at least one stress protein selected from the group consisting of Hsp90, Hsp70, Hsp25-27 and P-glycoprotein. More preferably, the levels of several or all of these proteins are elevated.”

#### **Claim rejections under 35 USC 103(a)**

The Patent Office rejected claims 16-20 and 23-25 under 35 USC 103(a) as being unpatentable over Li et al. (U.S. Pat. No. 5,830,177) in view of Jimenez et al. (U.S. Pat. No. 5,486,509).

Examiner argued as follows: “The Li et al. patent teaches compositions and treatment methods useful for the prevention of hair loss during chemotherapy. In a preferred embodiment, a nucleic acid comprising an expression vector capable of expressing human p-glycoprotein is administered to a subject (See Column 4, Lines 39-62). Methods of administration include the use of various carriers and incorporation into liposomes (See Column 5, Lines 16-23). Other methods of administration also include the utilization of electromagnetic radiation, including infrared radiation (See Column 5, Lines 58-66). Li et al. does not teach the administration of a method of treatment for the prevention of chemotherapy-induced alopecia between 2 and 24 hours before administration of a chemotherapeutic drug. Jimenez et al. teaches methods of inhibiting chemotherapy-induced alopecia (See Abstract)....Treatments for the prevention of chemotherapy-induced alopecia preferably administered once or twice daily beginning 5 to 8 days prior

to the administration of a chemotherapeutic agent (See Column 4, Lines 13-31; and Examples)" Examiner explained that the Jimenez et al. patent stands for the concept that an anti-alopecic treatment must be given sufficient time for generating resistance prior to administration of a chemotherapy agent. The rejection of claims 16-20 and 23-25 under 103(a) is now moot because of the cancellation of these claims.

For the following reasons applicant believes that the above arguments are not applicable to the new claim set:

Independent claims 26 and 30 do not relate to a method of administering a nucleic acid comprising an expression vector capable of expressing human p-glycoprotein. The claims specifically describe a method of heat treatment for preventing alopecia resulting from a subsequent exposure of hair follicles to a chemotherapy agent. Whereas "p-glycoprotein" appears in claim 30, it is not in the context of a delivery of a gene. As is also explained in the specification, p-glycoprotein synthesis is heat-induced in several organisms. Hence, increased levels of endogenous p-glycoprotein are an indication that a stress protein response has been induced. Endogenous p-glycoprotein level in hair follicles is used in the method of claim 30 as one of several markers for assessing the effectiveness of the heat dose administered to the patient or mammalian animal in need of anti-alopecic treatment.

Regarding the argument that Li et al. relates to compositions and treatment methods useful for the prevention of hair loss during chemotherapy and that methods of administration also include the utilization of electromagnetic radiation, including infrared radiation, reference is made to the explanation appearing in Column 5, Lines 37-44 of the Li et al. patent: "The methods and apparatuses of the present invention are particularly useful in delivering photosensitizing, photoreactive and photoactivated agents into hair follicles and the subsequent use of electromagnetic irradiation to activate that compound (hereinafter all such photo-enhanced agents will be referred to as photosensitizing agents). Specifically, following or during administration of such an agent and vibration,

irradiation is applied to the treated surface." As this explanation makes clear, the methods in Li et al. alluded to by the Examiner concern activation by electromagnetic irradiation of photosensitizing agents that are previously or concurrently administered. Therefore, administration of a photosensitizing agent and activating irradiation are obligatorily linked aspects of the methods. Moreover, these methods concern cell ablation and do not foresee concurrent or subsequent administration of a chemotherapeutic drug. Claims 26 and 30 of the subject invention specifically describe a method of heat treatment for preventing alopecia resulting from a subsequent exposure of hair follicles to a chemotherapy agent. Therefore, the methods suggested by Li et al., alone or in combination with Jimenez et al., and the methods of claims 26 and 30 are unrelated. Consequently, Li et al. and Jimenez et al. cannot render obvious the subject invention as described in claims 26 and 30.

In view of the foregoing remarks and amendments to the claims, Applicant believes that the claims currently before the Examiner are in condition for allowance, and notice of such action is respectfully requested. Examiner is cordially invited to call Applicant at 41-21-728-0320 if clarification is needed or if Examiner believes a telephone interview would expedite the prosecution of the subject application.

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Respectfully Submitted,



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